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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
10/28/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/525,011	NATUNEN ET AL.	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *87-134,137 and 140-157* is/are pending in the application.

4a) Of the above claim(s) *87-131 and 142-147* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *132-134,137 and 140-157* is/are rejected.

7)☒ Claim(s) *154 and 157* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed August 20, 2010 in response to the Office Action of February 22, 2010, is acknowledged and has been entered. Claims 87-134, 137, and 140-157 are pending. Claims 148-157 are new. Claims 132, 134, and 140 are amended. Claims 135, 136, 138, and 139 are canceled. Claims 87-131 and 142-147 remain withdrawn. Claims 132-134, 137, and 140-157 are currently being examined.

Claim Objections

2. Claim 154 is objected to because of the following informalities: The claim recites a method step although the elected and examined invention is a product. The claim will be withdrawn as being drawn to a non-elected invention if not amended, however, for the sake of compact prosecution, Examiner will not withdraw in this office action because Examiner believes Applicants intended to recite: "the composition according to claim 132, wherein the enzyme substrate is capable of being transferred to terminal β-GlcNAc residue." Appropriate correction is required.

Claim 157 is objected to for the same reasoning above for claim 154. The claim recites a method step although the elected and examined invention is a product. The claim will be withdrawn as being drawn to a non-elected invention if not amended, however, for the sake of compact prosecution, Examiner will not withdraw in this office action because Examiner believes Applicants intended to recite: "the composition according to claim 132, wherein the enzyme substrate is capable of being transferred to a cell, tissue, or therapeutic protein." Appropriate correction is required.

New Rejection

(necessitated by amendments)

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 154 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 154 recites the limitation "**the modified monosaccharide**". There is insufficient antecedent basis for this limitation in the claim.

Maintained Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

NOTE: The rejection below is maintained and additionally addresses claim amendments.

4. **Claims 132-134, 137, 140, and 141 remain rejected and new claims 148-157 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.** The claim(s) contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection (see section 12 of the previous Office Action).

The claims now broadly encompass **any galactosyltransferase enzyme** that is i) engineered to transfer effectively 2-modified UDP-Gal(N) or UDP-Glc(N) or ii) any natural GalNAc and/or GlcNAc-transferase capable of transferring effectively 2-modified hexose from 2-modified UDP-Gal(N) and/or UDP-Glc(N). The claims are further drawn to: the glycosyltransferase has the function of transferring both 2-modified Gal(N) and Glc(N); the glycosyltransferase is animal or human derived engineered β4-galactosyltransferase; the glycosyltransferase is β4-GlcNAc and β4-GalNAc-transferase.

The specification discloses enzyme substrates 2-modified galactosamine with the formula UDP-GalN[-S-]-D, that can be transferred by the animal enzyme β1,4-Galactosyltransferase I (β4Gal-T1), wherein the enzyme has a specific mutation that allows transfer of the 2-modified galactosamine. The specification discloses that an enzyme was used based on the enzyme produced by Ramakrishnan and Qasba (J of Biological Chemistry, March 2002, 277:20833-20839). Ramakrishnan and Qasba teach this specific enzyme as bovine β4Gal-T1 with a mutation of tyrosine-289 to Leu, Ile, or Asn that enhances the enzyme activity, wherein Y289L exhibited Gal-NAc-transferase activity that was nearly 100% of its Gal-T activity (abstract). The specification discloses that human β4Gal-T1 can be used with the same mutation and such an enzyme is

capable of transferring of a monosaccharide unit modified to position 2 ([0155-0156]). The specification discloses that the enzyme catalyzed the *ex vivo* transfer of GalN-PEG-fluorescein groups from UDP-GalN-PEG-fluorescein to non-reducing terminal N-acetylglucosamine (GlcNAc) residues present in glycoprotein glycans of human tumor cells and tumor tissue sections (Example 13). The specification discloses the incorporation of carboxilic acid reagents into the 2-amino group of uridine diphosphogalactosamine, which are suitable for protein-compatible water-solution coupling of N-maleimido, aldehyde, and thiol group containing reagents or biologically active substances. The reagents were incubated in aqueous solution with a non-reducing terminal N-acetylglucosamine containing glycoconjugate and a modified galactosyltransferase enzyme similar to the one described by Ramakrishnan and Qasba (above), which resulted in the successful transfer of conjugation reagent-modified galactosamine residues to the glycoconjugates ([0276], Example 14). The specification discloses making UDP-GalN-biotin (Example 4). Labeling of terminal GlcNAc residues in oligosaccharides and tissue sections with UDP-GalN-biotin. N-(6-biotinamidohexanoyl) galactosamine can be transferred from UDP-GalN-biotin to a terminal GlcNAc containing acceptor with a recombinant β1,4-galactosyltransferase similar to the enzyme described in Ramakrishnan and Qasba (above). The specification does not disclose any other glycosyltransferases, other than bovine or human β4Gal-T1 with mutation Y289L, that would function as broadly claimed.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics

of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of galactosyltransferase enzyme that is "i) engineered to transfer effectively 2-modified UDP-Gal(N) or UDP-Glc(N) or ii) natural GalNAc and/or GlcNAc-transferase capable of transferring effectively 2-modified hexose from 2-modified UDP-Gal(N) and/or UDP-Glc(N)," "wherein the glycosyltransferase is capable of transferring both 2-modified Gal(N) and Glc(N)," "wherein the glycosyltransferase is animal or human derived engineered β4-galactosyltransferase," "wherein the glycosyltransferase is β4-GlcNAc and β4-GalNAc-transferase." Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that " [a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. At 1567, 43 USPQ2d at 1405. The court also stated that:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical

properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. Thus, the instant specification may provide an adequate written description of an engineered or natural galactosyltransferase that function as claimed, per Lilly by structurally describing representative galactosyltransferases or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe the galactosyltransferases useful in the claimed invention in a manner that satisfies either the Lilly or Enzo standards. Although the specification discloses enzyme substrate 2-modified galactosamine with the formula UDP-GalN[-S-]-D that can be transferred by the human or bovine enzyme β1,4-Galactosyltransferase I (β4Gal-T1) with a specific mutation Y289L that allows transfer of 2-modified galactosamines, this does not provide a description of the broadly claimed galactosyltransferases that function as claimed that

would satisfy the standard set out in Enzo because the specification provides no structural features coupled to the claimed functional characteristics.

Further, the specification also fails to describe the galactosyltransferases that function as claimed by the test set out in Lilly because the specification describes only human or bovine enzyme β1,4-Galactosyltransferase I (β4Gal-T1) with a specific mutation Y289L that allows transfer of 2-modified galactosamine. Therefore it necessarily fails to describe a representative number of such species.

Thus, the specification does not provide an adequate written description of the broad genus of galactosyltransferases that function as claimed that is required to practice the claimed invention.

Response to Arguments

5. Applicants argue that the terms "enzyme substrate" and "transferring enzyme" are now limited to more clearly conform to the specific embodiments disclosed in the application as filed. Applicants argue that those of skill in the art would understand that Applicants were in possession of the claimed invention at the time of filing (p. 16-17).

The claims are now amended to recite the genus of enzyme substrates: 2-modified Gal(N) or 2-modified Glc(N) comprising UDP-Gal(N) or UDP-Glc(N), and the specification provides adequate written description to support the genus of substrates as amended.

With regards to the galactosyltransferases, the arguments have been considered but are not found persuasive because the claims are still broadly drawn to galactosyltransferases that are engineered or natural Gal(N) or Glc(N) transferases with unknown structure, and the specification and claims do not define the structural features commonly possessed by members of the broad genus that can distinguish it from others. There is no recitation or disclosure of structural features common to the members of the galactosyltransferase genus or which features constitute a substantial portion of the genus. The specification and claims do not identify which structural features are conserved among the galactosyltransferases, or which structures constitute a substantial portion of the genus in order for one to visualize or recognize the identity of the members of the genus, hence the written description for the genus of galactosyltransferases in the claimed composition do not meet the standards of Lilly. Although the specification discloses a single species of human or bovine enzyme β1,4-Galactosyltransferase I (β4Gal-T1) with a specific mutation Y289L that allows transfer of a 2-modified galactosamine, the claims are still broadly drawn to any galactosyltransferases that are either "engineered" to transfer 2-modified Gal(N) or Glc(N) from 2-modified UDP-Gal(N) or UDP-(glc(N), or that are "natural" GalNAc and/or GlcNAc-transferases "capable of transferring effectively 2-modified hexose from 2-modified UDP-Gal(N) and/or UDP-Glc(N)," and that are "animal or human derived engineered" β4-galactosyltransferases; and are β4-GlcNAc and β4-GalNAc-transferases. Although Applicants may argue claims limited to β4-galactosyltransferases and β4-GlcNAc and β4-GalNAc-transferases are supported in the specification, the

specification only provides a single species of β1,4-Galactosyltransferase I (β4Gal-T1) with a specific mutation Y289L that functions as required by the claims. Other than this single exemplary species of galactosyltransferase, there are no specific structures, identifying characteristics, partial or complete structures, or functional characteristic coupled with a known or disclosed structure for the broad genus of galactosyltransferases as recited in the claims, hence the specification does not provide adequate written description according to the standards of Enzo. Applicants were not in possession of the broadly claimed genus at the time of filing.

6. All other rejections recited in the Office Action mailed February 22, 2010 are hereby withdrawn in view of amendments.

7. **Conclusion:** No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. ' 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY

PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on 571-272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Primary Examiner, Art Unit 1642